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#### Remarks

This is in response to the Final Office Action mailed November 21, 2005. (Paper No./Mail Date 1105). Applicant notes with appreciation the Examiner's careful review of the previously-presented amendments and arguments. As set forth in the Office action, the grounds for rejection set forth in the First Office action have been withdrawn.

In the present Office action, the Examiner has rejected a number of the claims under § 102(a) as anticipated by Porscheddu and has rejected all of the claims as obvious in view of Porscheddu and Stadler or in view of Daga and Santagada and Stadler.

As a point of clarification, the Examiner has used the phrase "being anticipated" twice with respect to the § 103 rejections and Applicant assumes that the Examiner meant to use the term "obvious." Applicant will proceed under this assumption, subject to any further comment from the Examiner.

#### The Anticipation Argument Based Upon Porscheddu

Porscheddu cannot be properly applied as a § 102 reference because it fails to disclose all of the elements of the independent claims (e.g. Claim 1) within its four quarters. Specifically, Claim 1 as pending recites in its first two lines:

"A process for the solid phase synthesis of peptides, which comprises:  
(a) deprotecting a first amino acid linked to a solid phase resin by  
removing protective first chemical groups; . . ."

In contrast, Porscheddu specifically attaches the amino acid to a soluble polymer rather than a solid phase resin and carries out the deprotection reaction in solution rather than in a mixture of liquid and solid phases.

In particular, the first paragraph of the Porscheddu reference discusses certain perceived problems in solid phase synthesis ("its use has been limited by several problems"). Porscheddu then specifically offers soluble polymers as alternatives:

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“One of the possible alternatives to SPOS is the use of a soluble polymer as support. This polymer should be soluble in several organic solvents, so that the linked substrate may react in solution under standard conditions.”

Both quotes are from page 907, left-hand column, in the first paragraph of the text.

The Porscheddu reference offers a number of reasons why it prefers the soluble polymer over the solid phase method, with one example being the recovery of compounds from solution by precipitation at low temperature; e.g., page 907 right hand column, last full paragraph.

A number of other comments could be made about the disparity between the pending claims and the Porscheddu reference, but the clear cut difference between soluble and insoluble supports, combined with Porscheddu's explicit arguments against SPPS are sufficient to demonstrate that the soluble polymer teachings of Porscheddu are incongruent with the solid phase support techniques recited in the claimed invention. Thus, Porscheddu must be removed as a § 102 reference.

#### The § 103 Rejection Based on Porscheddu and Stadler

This combination fails as an obviousness combination for reasons similar to those under which Porscheddu fails as a § 102 reference. Namely, no logical reason exists to combine the solution-based technique of Porscheddu with the Stadler's solid phase technique (or any other solid phase technique). Stated differently, because Porscheddu (1) describes the disadvantages of SPPS and (2) teaches a soluble polymer as the preferred alternative, no logical reason exists to combine Porscheddu with a reference (Stadler) that emphasizes SPPS. Viewed objectively, the Porscheddu-Stadler combination serves no purpose other than as a hindsight reconstruction selected to match the pending claims.

#### The § 103 Rejection Based on Daga and Santagada and Stadler

This combination likewise fails to provide an appropriate method for peptide synthesis congruent with the pending claims.

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Daga's process tends to remove protecting groups from a side chain (an undesired result) when removing the protecting group from the alpha nitrogen. Protecting the side chain during N-alpha deprotection is, however, a necessary function in SPPS (otherwise coupling could occur at the unprotected side chain in the next step and thus preclude peptide growth). Because the capacity to remove N-alpha protecting groups while avoiding removing side chain protecting groups is a basic step in solid phase peptide synthesis, a reference that fails to protect the side chains cannot logically be combined with any reference to produce a working solid phase peptide synthesis. Such a reference specifically fails to render the pending claims obvious.

The favorable (and necessary) characteristic of a process that removes the N-alpha protecting group from an amino acid while leaving the side chain protecting group in place is referred to as being "orthogonal." Stated in those terms, Daga describes a deprotection process that is not orthogonal.

In considering this point, the Applicant draws the Examiner's attention to the deprotection reactions on page 5192 of the Daga reference and to the corresponding explanation in the first full paragraph in the left-hand column of page 5193. Specifically, reaction 13 on page 5192—deprotection of doubly-protected resin-based lysine—required eight cycles in order get 95 percent recovery. On page 5193 in the cited paragraph, however, Daga states,

"Nevertheless, when FmocProOMe was submitted to 10 cycles of irradiation and rest we observed 10 percent of deprotection."

In other words, Daga's desired removal of Cbz from the alpha nitrogen was accompanied by the undesired removal of Fmoc from the side chain.

This statement demonstrates the lack of an orthogonal function in Daga's deprotection step and thus makes Daga's particular method unsuitable for SPPS. Because the

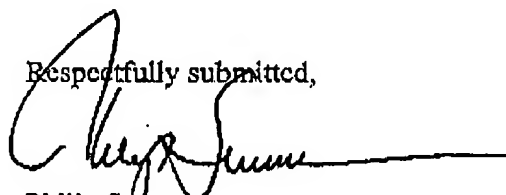
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Daga technique is unsuitable for SPPS, it cannot form any part of a logical combination against the claims.

Absent the Daga reference, the remainder of this combination must logically fail.

Accordingly, Applicant submits that the pending claims define over the rejections as applied in the November 21, 2005 Office Action and Applicant respectfully requests that these rejections be removed and the case passed to allowance at the earliest possible date.

Respectfully submitted,



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Philip Summa